I. The Office Action

The January 28, 2009 Final Office Action (the "Office Action") in this application:
1.) withdrew claims 23, 29 and 34-36;
2.) rejected claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 102 (b); and
3.) rejected claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 103(a).

Applicants request a three-month extension of time to reply to the Office Action, request continued examination (RCE) and Applicants respond as follows.

II. Claim amendments and cancellations

Independent claims 1 and 30 have been amended to specifically recite and point out that the monomer and oligomers are specifically provided in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant. Support for such limitations can be found at least in original claim 17, for example. Claim 19 has been amended to depend from claim 1, since the claim from which it previously depended has been canceled, and claim 27 is likewise amended to depend from claim 1, since the claim from which it previously depended had been canceled. Claims 17, 18 and 20 are hereby cancelled without disclaimer, prejudice or estoppel and solely to expedite prosecution. The Office Action has withdrawn claims 23, 29 and 34-36, stating that these claims are "...mutually exclusive from the originally presented claims which set forth that the acidity regulating component comprised a monomer and an oligomers derived from the same biodegradable polymer". Office Action, page 2. Applicants do not acquiesce to the propriety of any of the Office's issued rejections and may pursue canceled, excised, or originally claimed subject matter in one or more future applications.

III. Rejection of claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 102 (b)

Rejection of claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 102 (b) as being anticipated by Donovan (USP 6506399) or Donovan (USP 6312708). Applicants respectfully traverse this rejection.

The Court of Appeals for the Federal Circuit has stated that anticipation requires the presence in a single prior art reference of each and every element of the claimed

invention. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *Alco Standard Corp. v. Tennessee Valley Auth.*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic v. Genentech Inc.*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991) (citations omitted). To anticipate, the reference must teach "all of the limitations arranged or combined in the same way as recited in the claim." *Net MoneyIn v. Verisign*, Case No. 2007-1565 (Fed. Cir. 2008) This applies to all anticipation rejections made by the Office Action.

Presently, independent claims 1 and 30 are amended to recite that the monomer and oligomer are specifically derived from the same biodegradable polymer and said monomer and oligomers are provided in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant. A review of the disclosure of Donovan (USP 6506399) or Donovan (USP 6312708) fails to reveal or suggest a biodegradable neurotoxin implant that includes: a neurotoxin component associated with; a biodegradable polymer component; and an acidity regulating component effective in establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7, wherein the acidity regulating component comprises a monomer and an oligomer derived from the same biodegradable polymer; let alone where said monomer and oligomers are provided in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant (instant independent claim 1), nor a biodegradable neurotoxin implant including botulinum toxin type A and a biodegradable polymer component and an acidity regulating component effective in establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7, wherein the acidity regulating component comprises a monomer and an oligomer derived from the same biodegradable polymer and said monomer and oligomers are provided in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant (instant independent claim 30).

The Office Action, at page 5, lines 14-19, states that "Donovan et al disclose of the same [sic] biodegradable polymers as claimed, e.g., PLGA (See claims and

paragraph 84 of '399). Further, the PLGA polymer disclosed by Donovan inherently ***comprises*** oligomers an monomers of PLGA, as each are building blocks of the polymer molecule. Furthermore, oligomers and monomers of PLGA will be spontaneously generated in vivo as the polymer breaks down."

Respectfully, while both Donovan references disclose various polymers, such as, for example PLGA, nowhere can all of the limitations, arranged or combined in the same way as recited in the instant claims, be found and hence these references cannot anticipate the instant claims. It is noted that the instantly claimed biodegradable neurotoxin implant does not include a monomer and an oligomer derived from the same biodegradable polymer as a result of in vivo generation as the polymer breaks down; rather, the implant itself contains this acidity regulating component as an integral part/component of the implant. Accordingly, the PLGA polymer disclosed by Donovan does not inherently comprise oligomers and monomers of PLGA as components of the implant. Neither of the Office's cited references shows all of the elements arranged or combined in the same way as recited in the instant claims. For example and in one embodiment, the biodegradable polymer component and the acidity regulating component are blended together to form the implant (page 24, lines 25-27 of the specification).

The references do not show the claimed elements, biodegradable polymer with monomers and oligomers, in the novel relationship/same way as recited in the instant claims. The two Donovan references recite polymers but not monomers and oligomers initially furnished in addition to biodegradable polymers, and particularly the two Donovan references do not disclose or suggest them in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant, as all of the instant claims recite.

Thus, both Donovan references cannot anticipate the instant claims. It is respectfully requested that this rejection be withdrawn.

IV. Rejection of claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 103 (b)

The Office Action has rejected claims 1-15, 17-20, 24-25, 27, 30-31 and 33 under 35 U.S.C. 103 (b) as being unpatentable over Donovan in view of Schwendeman et al.

(U.S. Published Patent Application 20020009493). Applicants respectfully traverse this rejection.

It is respectfully pointed out that the combining of two or more references does not preclude an analysis of the references themselves, in order to determine, in the first instance, if even such a combination of references can be properly made (and if so found to be properly combinable, only thereafter are their resultant combined teachings and suggestions considered).

As previously asserted, Schwendeman et al. teaches away from using an acidity regulating component to create a microenvironment with a lowered pH. Schwendeman et al. disclosed methods which guard against degradation by acids. Thus in paragraph [0006] of Schwendeman et al. it states: "In accordance with the present invention, it has been discovered that, in many instances, the acids that are produced during biodegradation of PLGA can induce an irreversible inactivation or instability of biologically active agents, such as for example proteins, drugs, oligonucleotides and vaccine agents. It has also been determined that the addition of certain antacids, such as for example $MgOH_2$, to the system will not significantly reduce the acid-induced instability of the biologically active unless the polymer is prepared in a manner which results in the formation of an interconnected network of pores within the polymer."

Accordingly, the whole aim of Schwendeman et al. is to prevent acid degradation of a polymer, such as PLGA. Therefore, in order to arrive at the presently claimed invention, one of ordinary skill in the art would have to disregard this goal clearly enumerated in this reference. Schwendeman et al. directs a skilled artisan to go down one path: find ways to reduce or prevent acid-induced instability. To get to the presently claimed invention, the skilled artisan would have to go down another path: find ways to lower the pH to promote neurotoxin stability.

As has been held, "Proceeding contrary to the accepted wisdom of the prior art is strong evidence of nonobviousness. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 213 (Fed. Cir. 1983); *In re Hedges*, 783 F.2d 1038, 228 USPQ 685, 687 (Fed. Cir. 1986)". It is also noted that "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re

Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)". Clearly, modifying the teachings of Schwendeman et al. to include oligomers and monomers would be a modification that would render the prior art invention being modified unsatisfactory for its intended purpose. This undesirability (resulting in water-insoluble aggregates of the protein to be released, here BSA), is made clear in paragraph [0084] of Schwendeman et al. where "The possible cause for the increased BSA aggregation in PLGA85/15 microspheres relative to PLGA75/25 and PLA is the presence of more low MW species in PLGA85/15. The presence of monomers or oligomers can also produce acidic microclimate even before polymer degradation occurs.". Thus, it is seen that the proposed modification of the implant of Schwendeman et al. (supposedly suggested by the combination of Schwendeman et al. and Donovan) is clearly a case where such a modification (the purposeful inclusion of oligomers and monomers) renders the prior art invention being modified unsatisfactory for its intended purpose. Accordingly, then there is no suggestion or motivation to make the proposed modification.

In view of the teachings directing one of ordinary skill in the art against using the reference to achieve a stabilizing acidic environment, Applicants submit that one of ordinary skill in the art would not have combined Schwendeman et al. with Donovan et al. It is impermissible within the framework of 35 USC § 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to full appreciation of what such reference fairly suggests to one skilled in the art. Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc., 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986).

In addition, it is also noted that taking Schwendeman et al. and Donovan, alone or in combination, does not render obvious the particular biodegradable neurotoxin implants as presently claimed, where the acidity regulating component effective in establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7, wherein the acidity regulating component comprises a monomer and an oligomer derived from the same biodegradable polymer and said monomer and oligomers are provided in a range of about 0.1% (w/w) to about 30%(w/w) of the biodegradable neurotoxin implant, nor does this combination render

any of the dependent claim limitations obvious. Thus, it is respectfully requested that this rejection be withdrawn.

V. Conclusion

All issues raised in the final Office Action have been addressed and the application is believed to be in condition for allowance. A notice of allowance for pending claims 1-15, 19, 23-25, 27, 29-31, 33 and 37-39 is respectfully requested. Should any matter remain unresolved, the Examiner is invited to please call Applicants' representative at the number shown below.

The Commissioner is hereby authorized to charge any fees required or necessary for the filing, processing or entering of this paper, including a 3-month extension of time to reply to the outstanding Office Action and a request for continued examination (RCE) fee, or any of the enclosed papers and to refund any overpayment to deposit account 01-0885.

Respectfully submitted,

/Claude L. Nassif/

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Claude L. Nassif, Ph.D.
Reg. No. 52,061

Address all inquires and correspondence to:
Claude L. Nassif, Ph.D.
Allergan, Inc., Legal Department
2525 Dupont Drive, T2-7H
Irvine, CA 92612
Telephone: 714 246 6458
Fax: 714 246 4249